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Blood pressure targets in hemodialysis patients

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Guidelines on blood pressure control in dialysis patients are opinion-based. Effectiveness and risk analyses were not performed prior to implementation. We discuss this in the context of a study auditing blood pressure control in this population.

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Before clinical trials demonstrated the benefits of blood pressure (BP) control, the opinion prevailed that hypertension was 'essential' for end-organ perfusion, and that BP should not (and could not at the time) be lowered. In time, physicians accepted what life insurance actuaries had already known, that hypertension shortens lives. Evidence-based guidelines now instruct physicians to strictly control BP in high-risk groups. Most large-scale clinical trials exclude patients with end-stage renal disease, and thus guidelines targeting these patients are opinion-based and extrapolated from other populations. Because it seems reasonable that BP control should effectively reduce cardiovascular mortality in end-stage renal disease patients, most nephrologists attempt to follow this advice.

In 2002, the United Kingdom Renal Association Standards Committee recommended that the arbitrarily chosen BP standard be <140/90 mm Hg predialysis and <130/80 mm Hg postdialysis.[1] In 2005, the Kidney Disease Outcomes Quality Initiative (K/DOQI) Work Group on cardiovascular disease in dialysis patients (United States) agreed.[2] These guidelines were made in the absence of compelling clinical-trial evidence that lowering BP reduces mortality in the hemodialysis population. Therefore, both sets of guidelines carry a 'grade C' strength of recommendation, which states that "clinicians should *consider* following the guidelines for *eligible* patients," while recognizing that "the recommendation is based on *either weak evidence or on the opinions* of the Work Group, that *the practice might improve health outcomes*" (our emphasis). Because of this uncertainty, there is significant controversy surrounding the targeted pressure and the best method to achieve it. In fact, two other sets of K/DOQI guidelines (the 2004 guidelines on hypertension in chronic kidney disease and the 2006 update of hemodialysis adequacy guidelines),[3,4] do not recommend specific BP targets in hemodialysis patients. Instead, the K/DOQI hemodialysis adequacy guidelines focus on volume control, dietary sodium restriction, and avoidance of high dialysate sodium.

The hemodialysis adequacy guidelines highlight the importance of limiting sodium intake. As is eloquently pointed out by Tomson and others, fluid restriction without sodium restriction is worthless, because sodium intake drives thirst.[5] The difficulty in this approach remains convincing individual patients to alter their diet to avoid sodium, which is ubiquitous in many diets. While sodium has insidiously increased in processed foods, and sodium-rich 'fast foods' have become more readily available, dialysis units have also gradually increased dialysate sodium concentrations to reduce symptoms of cramping and hypotension. This combination of circumstances makes sodium removal during a dialysis session even more difficult.

The currently available alternatives using conventional hemodialysis are antihypertensive medications and aggressive ultrafiltration. In the typical dialysis unit, ultrafiltration consists of the removal of 2–4 liters over 4 hours (or less time), performed in a similar fashion three times weekly against variable dialysate sodium concentrations. As we have become accustomed to this routine, we have also become progressively less aware of the nonphysiologic nature of the dialysis process and how this routine developed for logistic and economic reasons rather than for optimal patient care. The frequent fluid shifts during hemodialysis and inability to rapidly compensate can result in intradialytic hypotension, bolus fluid resuscitation, and inability to achieve true dry weight. Because of the higher dialysate sodium concentration, the amount of sodium removed during dialysis is dependent on convection rather than diffusion. Depending on the individual patient's serum sodium concentration, the dialysate sodium concentration, and the volume of ultrafiltrate, sodium may actually be gained rather than removed during a dialysis session. In those patients who are unable or unwilling to comply with dietary restrictions, it may be impossible to remove the prescribed volume during a 4-hour session. These limitations are systematic and entrenched in the present culture of health-care delivery, but ongoing studies may challenge this standard. Frequent nocturnal dialysis may reduce BP in a larger percentage of patients, reverse left-ventricular hypertrophy, and hopefully even improve mortality rates.[6]

Davenport *et al.*[7] (this issue) investigated the effects of these targets on BP control and hypotensive events in London dialysis units in a 1-week observational study. The authors highlight the difficulty of achieving these guideline goals and the cost of such achievements. In the 11 units studied, the practice patterns of individual physicians varied widely. Forty-two percent of patients achieved postdialysis BP targets, and antihypertensive medications may have made the difference. Units with a higher per capita antihypertensive prescription rate also experienced the most success in meeting postdialysis BP goals.

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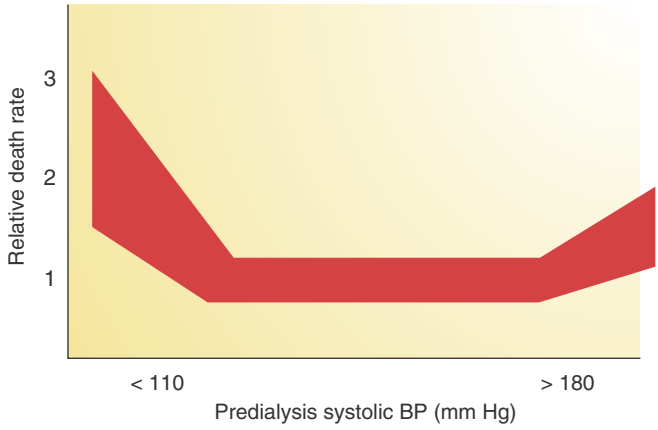

Figure 1 | Basic relationship of blood pressure (BP) to mortality in dialysis patients, as obtained from observational studies.

The price of achieving the targeted pressure may be intradialytic hypotension, as centers with a higher percentage of patients at BP goal also had a significantly higher rate of hypotensive episodes, defined as intradialytic fluid resuscitation. Many more patients probably were treated for intradialytic hypotension by simple cessation of ultrafiltration, but these data were not captured. Because of the observational nature of this study, the number of patients achieving BP goals also reflects a selection bias, as patients were not screened on the basis of the presence or absence of hypertension and/or need for antihypertensive medications. Thus, a significant percentage of the patients 'achieving' the goal BP are probably not chronically hypertensive and are not in the group targeted for BP reduction. These subjects may also contribute heavily to the number of patients requiring intradialytic fluid resuscitation, confounding the argument that trying to achieve the BP targets results in hypotension. In our opinion, the study does not support the guideline targets.

Large observational studies describe a U-shaped mortality (Figure 1) curve with regard to BP in dialysis patients.[8–10] Not only do they fail to demonstrate a correlation between worse outcome and significant hypertension, but they demonstrate increased mortality at lower BP. One such study used to support BP targets reveals an increased risk of cardiac hypertrophy with increasing BP but still demonstrates the paradoxically increased mortality rate in the lower BP range.[11] Quoting the authors, "low, not high, BP was associated with earlier death independently of age, diabetes, ischemic heart disease, anemia and hypoalbuminemia." Because of the observational nature of these studies, confounding factors leave us uncertain. Is the hemodialysis population truly unique in that hypertension somehow provides protection against dialysis-related adverse events? That argument would cast aside all the intervention trials in other populations. On the other hand, there seems to be some validity to this argument. Several large trials in hemodialysis patients have recently failed to show any mortality benefit for rational treatment goals such as raising hemoglobin levels, increasing the dose of dialysis, and prescribing statins or antioxidants.

With the paucity of trial data in the guideline-oriented practice of today, the work groups are faced with a dilemma. If a BP target is absent from the guidelines, then hypertension may receive inadequate medical attention. If BP targets are set too low, then nephrologists may expose their patients to an increased risk of intradialytic hypotension or other adverse events in an attempt to appease oversight committees or to attain pay-for-performance rewards.

Furthermore, guidelines based on 'grade C' strength of recommendation should at best be considered only recommendations and do not warrant a performance measurement. In proper medical-guideline development, risk analyses precede implementation. The study by Davenport *et al.*[7] should have been performed before the implementation. Effectiveness research is critical for any guideline and must address the possibility that physicians may not execute the recommendations if they do not think that the practice will achieve the desired goal (a concept called lack of expectancy outcome).

If survival is the desired outcome in hemodialysis patients, why lower BP? Guidelines must not contradict other guidelines or cause confusion. We discussed this problem above. Taking all these issues into account, it becomes clear that we less need guidelines on BP control in dialysis patients than we need adequately powered clinical trials to determine the risks and benefits of BP control. The K/DOQI guidelines on hemodialysis adequacy have instead taken a reasonable approach by excluding any BP goals and focusing on patient education and prevention of hypertension with dietary sodium restriction.

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